



SEQUENCE LISTING

<110> Delansorne, Rémi
Bonnet, Paule
Paris, Jacques

<120> Pharmaceutical compositions based on alpha-cyclodextrin
for the oral administration of LH-RH analogues

<130> H20058-5US

<140> 09/787,436
<141> 2000-03-17

<150> PCT/EP99/07389
<151> 1999-09-23

<150> EP98402403.4
<151> 1998-09-30

<160> 7

<170> PatentIn Ver. 2.1

<210> 1
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:LH-RH analogue

<220>
<221> SITE
<222> (1)
<223> Xaa is pGlu, D-pGlu, Sar, AcSar, Pro, Ser, D-Ser, Ac-D-Ser,
Thr, D-Thr, Ac-D-Thr or an optionally substituted and/or acylated
aromatic D-amino acid

<220>
<221> SITE
<222> (2)
<223> Xaa is His or an optionally substituted aromatic D-amino acid

<220>
<221> SITE
<222> (3)
<223> Xaa is an optionally substituted aromatic L- or D-amino acid

<220>
<221> SITE
<222> (4)
<223> Xaa is Ala, Ser, D-Ser, MeSer, Ser(Obut), Ser(OBzl) or Thr

<220>
<221> SITE
<222> (5)
<223> Xaa is an optionally substituted aromatic L-amino acid
or an optionally substituted basic L- or D-amino acid

<220>

<221> SITE
 <222> (6)
 <223> Xaa is Gly, (S)-spirolactam-Pro, D-Pro, D-Ser, D-Thr, D-Cys, D-Met, D-Asn, D-Pen, D-(S-Me)Pen, D-(S-Et)Pen, D-Ser(OBut), D-Asp(OBut), D-Glu(OBut), D-Thr(OBut), D-Cys(OBut), D-Ser(OR1) where R1 is a sugar moiety

<220>
 <221> SITE
 <222> (6)
 <223> Xaa is an aza-amino acid, D-His which may be substituted on the imidazole ring by a (C1-C6)alkyl, a (C2-C7)acyl or a benzyl group, an aliphatic D-amino acid with a (C1-C8)-alkyl or a (C3-C6)cycloalkyl side chain

<220>
 <221> SITE
 <222> (6)
 <223> Xaa is an optionally substituted aromatic D-amino acid, D-cyclohexadienyl-Gly, D-perhydronaphthyl-Ala, D-perhydrodiphenyl-Ala
 or an optionally substituted basic L- or D-amino acid

<220>
 <221> SITE
 <222> (7)
 <223> Xaa is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C1-C4)alkyl group optionally substituted by one or several fluorine atoms

<220>
 <221> SITE
 <222> (8)
 <223> Xaa is an optionally substituted basic L- or D-amino acid

<220>
 <221> SITE
 <222> (10)
 <223> Xaa is GlyNH2, D-AlaNH2 or azaGlyNH2

<400> 1
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Pro Xaa
 1 5 10

<210> 2
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:LH-RH analogue

<220>
 <221> SITE
 <222> (1)
 <223> Xaa is pGlu, Sar or AcSar

<220>
 <221> SITE
 <222> (3)

<223> Xaa is an optionally substituted aromatic L-amino acid

<220>

<221> SITE

<222> (4)

<223> Xaa is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr

<220>

<221> SITE

<222> (5)

<223> Xaa is an optionally substituted aromatic L-amino acid

<220>

<221> SITE

<222> (6)

<223> Xaa is Gly, (S)-spirolactam-Pro, D-Pro, D-Ser, D-Thr, D-Cys, D-Met, D-Pen, D-(S-Me)Pen, D-(S-Et)Pen, D-Ser(OBut), D-Asp(OBut), D-Glu(OBut), D-Thr(OBut), D-Cys(OBut), D-Ser(OR1) where R1 is a sugar moiety

<220>

<221> SITE

<222> (6)

<223> Xaa is an aza-amino acid, D-His which may be substituted on the imidazole ring by a (C1-C6)alkyl or a benzyl group, an aliphatic D-amino acid with a (C1-C8)alkyl or a (C3-C6)cycloalkyl side chain,
an optionally substituted aromatic D-amino acid

<220>

<221> SITE

<222> (6)

<223> Xaa is D-cyclohexadienyl-Gly, D-perhydronaphthyl-Ala, D-perhydrodiphenyl-Ala or an optionally substituted basic D-amino acid

<220>

<221> SITE

<222> (7)

<223> Xaa is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C1-C4)alkyl group optionally substituted by one or several fluorine atoms

<220>

<221> SITE

<222> (8)

<223> Xaa is an optionally substituted basic L-amino acid

<220>

<221> SITE

<222> (10)

<223> Xaa is GlyNH2 or azaGlyNH2

<400> 2

Xaa His Xaa Xaa Xaa Xaa Xaa Xaa Pro Xaa
1 5 10

<210> 3

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:LH-RH analogue

<220>

<221> SITE

<222> (1)

<223> Xaa is pGlu

<220>

<221> SITE

<222> (3)

<223> Xaa is as defined for SEQ ID NO:2

<220>

<221> SITE

<222> (5)

<223> Xaa is as defined for SED ID NO:2

<220>

<221> SITE

<222> (6)

<223> Xaa is as defined for SED ID NO:2

<220>

<221> SITE

<222> (7)

<223> Xaa is Leu, Tle, Nle, Hol, Npg, Cha or Ada, which may
be N-alpha-substituted by a methyl or ethyl group
optionally substituted by one or several fluorine atoms

<220>

<221> SITE

<222> (10)

<223> Xaa is as defined for SEQ ID NO:2

<400> 3

Xaa	His	Xaa	Ser	Xaa	Xaa	Xaa	Arg	Pro	Xaa
1				5					10

<210> 4

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:LH-RH analogue

<220>

<221> SITE

<222> (1)

<223> Xaa is pGlu

<220>

<221> SITE

<222> (3)

<223> Xaa is Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, lNal,
Bal, Pal, 4Pal or pClPhe

<220>

<221> SITE
 <222> (5)
 <223> Xaa is Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, 1Nal, Bal, Pal, 4Pal or pClPhe

 <220>
 <221> SITE
 <222> (6)
 <223> Xaa is (S)-spiolactam-Pro, Gly, D-Pro, D-Ser(Obut), D-Asp(Obut), D-Glu(Obut), D-Thr(Obut), D-Cys(Obut), D-His, D-His(Bzl), D-Ala, D-Leu, D-Tle, D-Nle, D-Hol, D-Npg, D-Cha, D-Phe, D-HPhe, D-Tyr, D-HTyr, D-Trp

 <220>
 <221> SITE
 <222> (6)
 <223> Xaa is D-2MeTrp, D-Nal, D-1Nal, D-Bal, D-Pal, D-4Pal, D-pClPhe D-cyclohexadienyl-Gly, D-perhydronaphtyl-Ala, D-perhydrodiphenyl-Ala or D-APhe optionally substituted by an aminotriazolyl group

 <220>
 <221> SITE
 <222> (7)
 <223> Xaa is Leu, Npg or Cha, which may be N-alpha-substituted by a methyl group

 <220>
 <221> SITE
 <222> (10)
 <223> Xaa is GlyNH2 or azaGlyNH2

 <400> 4
 Xaa His Xaa Ser Xaa Xaa Xaa Arg Pro Xaa
 1 5 10

 <210> 5
 <211> 10
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Description of Artificial Sequence:LH-RH analogue

 <220>
 <221> SITE
 <222> (1)
 <223> Xaa is pGlu

 <220>
 <221> SITE
 <222> (6)
 <223> Xaa is (S)-spiolactam-Pro, D-Leu, D-Ala, D-Nal, D-Phe, D-Ser(Obut) or D-Trp

 <220>
 <221> SITE
 <222> (7)
 <223> Xaa is Leu, MeLeu, Npg or MeNpg

 <220>

<221> SITE
<222> (10)
<223> Xaa is GlyNH₂, azaGlyNH₂ or -NC₂H₅

<400> 5
Xaa His Trp Ser Tyr Xaa Xaa Arg Pro Xaa
1 5 10

<210> 6
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:LH-RH analogue

<220>
<221> SITE
<222> (1)
<223> Xaa is pGlu, D-pGlu, Sar, AcSar, Pro thereof, Ser, D-Ser, Ac-D-Ser, Thr, D-Thr, Ac-D-Thr or an optionally substituted and/or acylated aromatic D-amino acid

<220>
<221> SITE
<222> (2)
<223> Xaa is an optionally substituted aromatic D-amino acid

<220>
<221> SITE
<222> (3)
<223> Xaa is an optionally substituted aromatic L- or D-amino acid

<220>
<221> SITE
<222> (4)
<223> Xaa is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr

<220>
<221> SITE
<222> (5)
<223> Xaa is an optionally substituted aromatic L-amino acid or an optionally substituted basic L- or D-amino acid

<220>
<221> SITE
<222> (6)
<223> Xaa is Gly, (S)-spirolactam-Pro, D-Pro, D-Ser, D-Thr, D-Cys, D-Met, D-Asn, D-Pen, D-(S-Me)Pen, D-(S-Et)Pen, D-Ser(OBut), D-Asp(OBut), D-Glu(O-But), D-Thr(O-But), D-Cys(O-But), D-Ser(O-R₁) where R₁ is a sugar moiety

<220>
<221> SITE
<222> (6)
<223> Xaa is an aliphatic D-amino acid with a (C₁-C₈)alkyl or a(C₃-C₆) cycloalkyl side chain, an optionally substituted aromatic D-amino acid
D-cyclohexadienyl-Gly, D-perhydronaphthyl-Ala, D-perhydrodiphenyl-Ala

or an optionally substituted basic L- or D-amino acid

<220>
<221> SITE
<222> (7)
<223> Xaa is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C1-C4)alkyl group optionally substituted by one or several fluorine atoms

<220>
<221> SITE
<222> (8)
<223> Xaa is an optionally substituted basic L- or D-amino acid

<220>
<221> SITE
<222> (10)
<223> Xaa is GlyNH2 or D-AlaNH2

<400> 6
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Pro Xaa
1 5 10

<210> 7
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:LH-RH analogue

<220>
<221> SITE
<222> (1)
<223> Xaa is Ac-D-Nal

<220>
<221> SITE
<222> (2)
<223> Xaa is D-pClPhe

<220>
<221> SITE
<222> (3)
<223> Xaa is D-Pal

<220>
<221> SITE
<222> (5)
<223> Xaa is Tyr, HTyr, MeTyr, MeHTyr, NicLys or IprLys

<220>
<221> SITE
<222> (6)
<223> Xaa is (S)-spiolactam-Pro, D-Arg, D-NicLys, D-IprLys, D-Cit, D-HCit or D-Asn

<220>
<221> SITE
<222> (7)

<223> Xaa is Leu, MeLeu, Npg or MeNpg

<220>

<221> SITE

<222> (8)

<223> Xaa is Arg, NicLys or IprLys

<220>

<221> SITE

<222> (10)

<223> Xaa is DAlaNH2

<400> 7

Xaa Xaa Xaa Ser Xaa Xaa Xaa Xaa Pro Xaa

1

5

10